DESIGNING FOR DEEP DECARBONIZATION: ACCELERATING THE U.S. BIOECONOMY

DESIGNING FOR DEEP DECARBONIZATION: ACCELERATING THE U.S. BIOECONOMY

Executive Committee

Dionysios Antonopoulos, Argonne National Laboratory

Adam Bratis, National Renewable Energy Laboratory

Mary Maxon, Lawrence Berkeley National Laboratory

Julie Mitchell, Oak Ridge National Laboratory

Malin Young, Pacific Northwest National Laboratory

Steering Committee

Gyorgy Babnigg, Argonne National Laboratory

Scott Baker, Pacific Northwest National Laboratory

Gregg Beckham, National Renewable Energy Laboratory

Héctor García Martín, Lawrence Berkeley National Laboratory

Katy Christiansen (chair), Lawrence Berkeley National Laboratory

Jon Magnuson, Pacific Northwest National Laboratory

Aindrila Mukhopadhyay, Lawrence Berkeley National Laboratory

Xiaohan Yang, Oak Ridge National Laboratory

TABLE OF CONTENTS

EXECUTIVE SUMMARY

Despite compounding impacts of climate change resulting from anthropogenic greenhouse gas emissions, global reliance on fossil-derived carbon for energy, industry, and agriculture continues to increase. Biomass resources and biotechnology offer opportunities across these sectors of the economy to provide net negative carbon technologies that will contribute to meeting the Biden Administration's 2050 goal of a net zero carbon emissions economy. Advancing technologies that can efficiently convert biomass to biofuels and bioproducts can simultaneously achieve decarbonization while supporting the expansion of the United States' bioeconomy and fostering job creation, particularly in disadvantaged rural and agricultural areas. Application of biotechnology to decarbonize transportation, industry, and agriculture remains limited due to technology barriers, development time, and cost. Overcoming the dominance of fossil-derived carbon sources requires new approaches and value propositions to accelerate the transition towards renewable resources for deep decarbonization driven by biotechnology.

On April 30, 2021, five DOE national laboratories hosted the *Designing the Bioeconomy for Deep Decarbonization* workshop to identify high-impact opportunities for biotechnology to decarbonize DOE-mission relevant sectors and forward-looking enabling technologies, including integration of automation and artificial intelligence and machine learning (AI/ML) techniques. **Near-term, high-impact opportunities discussed include the production of sustainable aviation fuels, high-performance fuel additives, performance-advantaged bioproducts, new hybrid biotechnology and chemical synthesis processes, increased above-ground CO_2 capture and below-ground carbon storage, and expanded replacements to animal-based protein.**

Biotechnology is a vital GHG reduction tool

Potential for U.S. CO_2e reductions per year in 2030
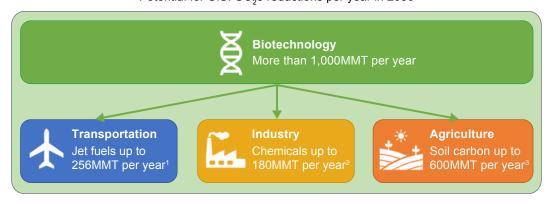
Figure 1: Potential for reductions in CO_2e from biotechnology-driven solutions, in millions of metric tons (MMT) per year, for selected sector opportunities identified by workshop participants. Projections are not limited by feedstock availability and based on a favorable policy environment that favors bio-based solutions.[1–3]

Jet fuels and high-performance fuel produced from renewable resources can replace petroleum-based products for transportation modes that will take longer to electrify or transition to alternative fuels, such as aviation. New products like plastics and industrial chemicals can be created from deconstructed biomass, which contains a range of constituents that are not present in fossil resources, to create a wide range of molecules and polymers that offer performance benefits like recyclability while reducing energy use and toxic byproducts. Through improved crops

and agricultural practices, plants that efficiently take up carbon dioxide from the atmosphere to direct it into soils can be turned into replacements for animal proteins, thus reducing carbon dioxide in the atmosphere, reducing methane from livestock, and meeting new market needs without the expansion of land-use change.

Strategic opportunities for biotechnology to reduce emissions

Rapid advances in biotechnology to reduce greenhouse gas (GHG) emissions: biological processes can effectively deconstruct heterogeneous and recalcitrant substrates like biomass and plastic, convert them to specific products with high selectivity, and perform safely at low temperatures and pressures compared to other industrial processes. When applied to reducing U.S. and global GHG emissions, biotechnology can replace a significant share of products and practices for transportation fuels and additives, manufacturing, and agriculture currently produced or powered by nonrenewable and/or unsustainable fossil resources. Advanced aviation fuels can reduce current GHG emissions from planes by 50–80%, while "recycling" the carbon dioxide that plants capture from the atmosphere through photosynthesis. Performance-advantaged polymers that are recyclable by design can substantially reduce both U.S.-based GHG emissions from manufacturing and plastics pollution in disadvantaged areas of the country and planet. Improvements to agriculture and silviculture can be used to store 25% more carbon in soils, captured through crops and trees, to remove GHGs from the atmosphere. Accelerating biotechnology-driven solutions to meet urgent needs to mitigate climate change can contribute to significant GHG reductions, decarbonization of sectors, new green jobs, and energy and environmental justice.

Biotechnology is rapidly evolving. Genome engineering was first enabled through the use of recombinant DNA, which was discovered in the late 1970s. Since that time, vast improvements in genome sequencing and DNA synthesis, combined with a range of genome editing technologies, have increased our ability to understand, control, and design biological systems at the genomic level. More recently, the emergence of CRISPR as a gene editing technology and the explosion in computational power have presented a massive opportunity to design and engineer biological systems with myriad possibilities for new products from sustainable biomass resources, including fuels for aviation, infinitely recyclable bioplastics, and techniques to enhance soil microbial communities to increase crop productivity. While there has been exceptional progress in biotechnology development, greater insight into the functioning and design of biological systems is only just beginning. Through the application of high-performance computers and new AI/ML methods, researchers are now able to examine extremely large, complex, and multivariate biological data in ways not possible before. From such techniques, new insights into the functioning of entire biological systems are possible. Systems-based understanding aided by AI/ML techniques, coupled with automated and iterative experimentation, is poised to yield unprecedented breakthroughs in the understanding of biology and accelerate biotechnology-driven solutions to market. While a handful of companies and research institutions — including those supported by DOE's Office of Science and Office of Energy Efficiency and Renewable Energy — are invested in this intersection, these resources are not widely available throughout the innovation ecosystem and require expanded, sustained, and targeted support that will enable the use of biotechnology for the rapid and sustainable deep decarbonization of transportation, industry, and agriculture.

Accelerating biotechnology with artificial intelligence, machine learning, and automation

To take advantage of the opportunities afforded by integration of automation with AI/ML computational techniques, dedicated efforts that bring together biological research, data science, computer science, and engineering are needed. Historically, biotechnology and biological research have relied on investigator-led, hypothesis-driven experimental design. While this targeted research

has illuminated the functions of the biological world around us and enabled elegant biological engineering, we now have the computational and experimental tools to examine biological concepts in a much broader and multivariate context than ever before, creating opportunities to efficiently design new biological systems through biotechnology. The challenges of integrating biotechnology with AI/ML and automation can be overcome through support for multidisciplinary, high-impact research and development for near-, mid-, and long-term solutions. Rather than treating each element as a separate part of research and development, teams that bring together researchers across disciplines can design experiments that capture the maximum data possible in formats that are ready for artificial intelligence and machine learning. These computational approaches can be employed to design and re-design experiments based on iterative learnings to improve the power of predictive models in a self-reinforcing cycle. Researchers that work to bring together the technologies needed and that develop new approaches to save time, effort, and money through miniaturization and automation can expedite the time from experiments to deployable technologies. This in turn will accelerate the transition to clean transportation, industry, and agriculture while reducing GHG emissions, storing carbon for long periods of time, and reducing the environmental harms from these sectors in disadvantaged areas of the U.S.
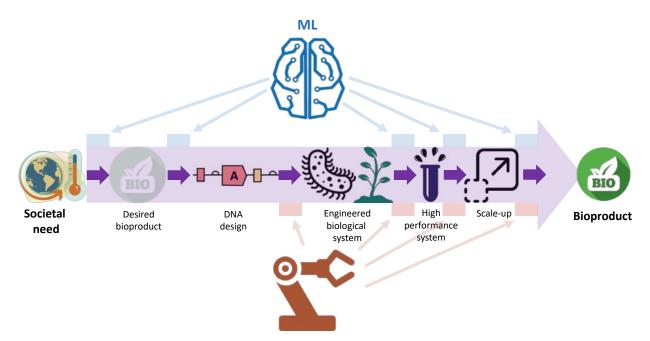

Figure 2: Opportunities for disruptive application of machine learning (ML) and automation in bioengineering for contributing to societal needs, such as fighting climate change.

To expand upon the findings of the April 30, 2021 workshop, a series of implementation workshops over the next four months will identify scientific, technical, workforce, and commercialization opportunities and inform a strategy for how DOE support for purposeful efforts at the intersection of biotechnology, computing, and automation can accelerate the impacts of new technologies in fuels and additives, industrial production of chemicals and polymers, agricultural practices for biomass feedstocks, and soil carbon storage. Connecting to these opportunities, the proposed workshops would cover: **1)** biological grand challenges that would enable rapid progress across sectors (e.g., solving "holy grails" of biology that are essential for improved design capabilities), **2)** technical challenges, opportunities, and strategies to integrate artificial intelligence, machine learning, and automation with biotechnology, **3)** integration of systems analysis including technoeconomic analyses and life cycle assessments for driving experimentation and learning, and **4)** workforce development and incentives and technology transition for new approaches.

APPENDIX A:

DESIGNING THE BIOECONOMY FOR DEEP DECARBONIZATION WORKSHOP FINDINGS AND PROPOSED NEXT STEPS

Transportation

High-impact opportunities

Transportation currently accounts for about a third of the yearly U.S. GHG emissions (including 1.8 Gt of CO_2e out of a total of 5.4 Gt)[4] While electrification of the light-duty vehicle fleet is expected to be the main course for decarbonization of this sector, there is a significant fraction of difficult-to-eliminate emissions. Among them, the highest impact opportunities are:

- Aviation fuels,

- Long distance road transport fuels and shipping fuels,

- CO_2 capture and reutilization, and

- Fuel blends.

How much GHG can we offset? Aviation contributed to 9% of the GHG emissions of the transportation sector in 2018.[5] This percentage is projected to grow as light-duty road vehicles become electrified. Long-distance road-transport fuels for medium- and heavy-duty trucks and shipping constituted 20–22% of the transport sector GHG in 2018. This sector also benefits from biotechnology-based replacements, but has alternate solutions available including electrification. Aviation remains the most challenging sector to electrify. In 2018, aviation fuels accounted for 0.175 Gt CO_2e and represents the amount of GHG that can be offset using bio-based aviation fuels. Complete offsetting of this GHG portion relies upon our ability to recapture CO_2.

Will it be cost effective? Achieving high titers, rates, and yields during bioproduction is critical for economically viable biofuels. In a promising analysis for advanced aviation fuels, a 50% maximum theoretical yield in an efficient conversion process (e.g., low O_2 use), separations, recovery, and reuse of effluents (e.g., CO_2 capture) coupled with higher-value bioproducts, could result in a cost-effective scenario. CO_2 capture from industrial processes is also a promising venue for transportation fuel production.[6]

Is there enough lignocellulose to make so much biofuel? A 2016 modeling and analysis of the DOE Billion-ton Bioeconomy initiative estimated that by 2030, producing 12.3 B GGE jet fuel from biomass was possible and could reduce emissions by 448 MMT/y.[7]

Why biotechnology is the right solution at the right time for this opportunity

- Bioconversion offers opportunities for specific hydrocarbon targets for advanced blends that leverage the strengths of biology, and that can convert complex carbon sources with high specificity. Examples are selective branching positions, unsaturation, and cyclization that result in optimal fuel properties. Life-cycle analysis of such advanced biojet fuels with tailored high-energy density show them to be cost-effective at 50% max theoretical yield based on process efficiency, and provide at least 50% reduction in GHG-intensity relative to petroleum derived jet fuel.[6]

- Biotechnology also provides routes to biofuels that are compatible with existing fuel distribution infrastructure.

- A range of fuel blend agents are also accessible via bioconversion, as drop-ins for targets that have high carbon or ecological footprint, or new targets with tailored properties.

- Lignocellulose feedstocks ideal for biotechnological conversion are abundant (DOE billion ton report).

- Lignocellulose-based transportation fuel production methods that are agnostic to specific feedstocks are implementable in a distributed manner and would boost job growth in rural areas.

- Bioconversion also provides access to key intermediates that are already known to meet high productivity metrics (e.g., ethanol, short chain alcohols), and coupled with chemical conversion for final fuel production. This also provides a form of funneling for disparate sustainable carbon sources to high-shelf-life intermediates, and a clear immediate incentive to use lignocellulose.

- Biological systems able to capture and convert CO_2 already exist in nature. CO_2 recapture is an essential aspect of GHG reductions.

Barriers and gaps that can be addressed with DOE investment/focus

- Engineering microbes is a costly multiyear endeavor.

- The pharma paradigm for metabolic engineering is too costly for the biofuels case.

- Highly efficient, biomass-agnostic, cost-effective deconstruction approaches are required.

- Improved ability to engineer cells (particularly non-model organisms for lignin conversion) is needed.

- Specific barriers to strain engineering:

    ° Genetic tools for non-model organisms are not available.

    ° Comprehensive autotrophic gene annotation is lacking.

    ° CO_2 stream utilization has very low efficiency.

    ° Energy source required for CO_2 utilization.

- Hydrocarbon based biofuels and relevant booster molecules are often toxic to the conversion (e.g., microbial) platform.

- It is non-trivial to predict the outcome of bioengineering attempts.

- Scale-up is currently more of an art than a science, and remains a bottleneck for commercialization of biologically produced targets.

- Separation requires dedicated effort and is also dependent upon the final product.

- Testing for biofuels requires large quantities of the compound that, even when commercially available, is cost-prohibitive.

- We need predictive tools to understand required properties of novel structures, so as to down-select scale-up and testing to smaller sets of targets, and to fully leverage the specificity afforded by biological conversion.

- Fuel standards and coordination of major players across the value-chain are required for boosters to be commercially viable.

- There are not enough incentives for innovation in biotechnology for development of biofuel production platforms. Biofuels cost efficiencies are challenging to meet without key policies.

Industry

High-impact opportunities for each sector

For the Industry sector, the plenary talk and breakout sessions focused on the role of biotechnology and enabling cross-cutting technologies (automation, AI/ML) for decarbonization of the bioeconomy in three impactful topic areas: **1)** polymers, additives, and materials; **2)** agrochemicals and fertilizers; and **3)** hybrid biological-chemical processes. Clearly, there are many chemicals and materials that can be produced by biotechnology and the combined impacts are highlighted below.

- Petrochemicals account for >30% of the total energy use in the United States, so the potential impact of biotechnological processes to offset the production of these chemicals is enormous.[8]

- Hybrid processes using the best of biotechnology and chemical catalysis promise high atom and energy efficiency and access to a greater diversity of chemical and material synthetic space for increased economic competitiveness with decreased environmental impacts. The DOE has funded substantial, impactful R&D to this end in the context of biofuels and biochemicals.

- The replacement of single-use petrochemical plastics with performance-advantaged polymers that are recyclable by design would substantially reduce both U.S.-based GHG emissions from manufacturing and plastics pollution in disadvantaged areas of the country and planet (e.g., U.S. annual ethylene and propylene production is 46 million MT).[9,11]

- The usage lives of carbonaceous materials (plastics, carbon fiber, building structural materials) are long and they are not combusted like fuels, so carbon sequestered in biomaterials has a multiplicative impact.

- Replacing natural gas–driven nitrogen fixation (120 million MT per annum globally) with biotechnology-based nitrogen fixation would prevent consumption of 3–5% of the world's

annual natural gas production and reduce release of other GHGs (e.g., N_2O, 7% of U.S. GHG) and reduce pollution in economically disadvantaged regions of the country from production and over-application of fertilizer.[12]

Why biotechnology is the right solution at the right time for this opportunity

- Fundamentally, biological systems generate all of the valuable carbon-based products that we need; whereas fossil carbon sources are ancient biological carbon, biotechnology uses renewable biological carbon.

- Biotechnology generates pure products with high specificity, which is important, for example, in producing single- or dual-molecule products like plastics.

- Biotechnology has experienced a revolution in the last two decades — in the form of genomics and synthetic biology — that enables data-intensive approaches for the design and implementation of new processes.

- Developments in AI/ML can be leveraged with increasingly vast amounts of biological data to accelerate scale-up and deployment of biotechnological advances.

- Increasingly sophisticated approaches inherent in hybrid processes require advanced modeling, multi-disciplinary expertise, and AI/ML.

- There are an increasing number of biofoundries in the U.S. and globally that are allying to implement biosynthetic and bioprocessing solutions for the bioeconomy.

- Understanding and predicting complex interactions of organisms (e.g., microbiomes, plant-bacteria-fungi) requires advanced omics, modeling, and AI/ML to enable robust implementation of advanced biosystems for increasing carbon, nitrogen, phosphorus, and water use efficiency in agriculture and bioprocessing.

Barriers and gaps that can be addressed with DOE investment/focus

- Disrupting technological silos by encouraging biology/chemistry/engineering/data-science approaches to process and product development.

- Development of hybrid processes in a predictive process modeling context to match rates, process conditions, and purity requirements for the most efficient chemicals and materials syntheses.

- Developing scalable and diverse process-compatible organisms, enzymes, and catalysts requires large-scale, multidisciplinary approaches equipped with advanced instrumentation and high-performance computing resources.

- More high-quality data across process scales for AI/ML synthetic approaches and TEA/LCA-driven pathway selection.

- Provide an emphasis on diversity, equity, and inclusion (DEI) in workforce development in this multidisciplinary endeavor of building a bioeconomy.

Cross-cutting approaches needed to address the barriers

- Expertise in development of AI/ML in other sectors of the US economy provides the depth of human resources that need to be leveraged for biotechnology-specific applications.

- Development and application of automation and microfluidics across biotechnology (i.e., DNA synthesis and assembly, to culturing and testing of engineered microbes) will increase the quantity of high-quality data for AI/ML approaches.

- AI/ML coupled to TEA/LCA modeling can be used to design and implement the best hybrid approaches to chemicals and materials, including hybrid biological/chemical retrosynthesis pathways.

Agriculture

High-impact opportunities for this sector

During the breakout sessions, the Agriculture group, composed of 10 members from national labs, universities, and industries, discussed the role of biotechnology and cross-cutting technologies (e.g., artificial intelligence, machine learning) in carbon reduction mediated by agricultural systems, with a focus on four topics: **1)** Carbon storage in soils through silviculture and agriculture for carbon negative economy; **2)** traditional food replacements with lower GHG emissions such as plant-based meats; **3)** direct production of chemicals in engineered plants; and **4)** biological approaches to increase nitrogen-use efficiency and reduce GHG emissions. The breakout discussions have identified the following high-impact opportunities:

- Improvements to current silviculture and agriculture practices could lead to ~25% potential increase in carbon sequestration.[13,14]

- Improving nitrogen-use efficiency in crop plants could potentially reduce up to 1/2 of synthetic nitrogen fertilizer waste, consequently reducing GHG and CO_2 emissions (0.5% and 0.7%, respectively) as well as saving US$100 billion globally per year.[15]

- Plant-based and cell culture–based meat could partially replace traditional livestock production, which generates ~7.1 gigatonnes CO_2-eq per year, accounting for 14.5% of global anthropogenic GHG emissions.[16]

- There is great economic potential for utilization of carbon captured by engineered crop plants. For example, sugarcane could be engineered to produce very large amounts of biodiesel, with a yield (~6700 liters/ha) much higher than soybean (~500 liters/ha).[17]

- GHG can be significantly reduced by improvement in agricultural soil management, which accounts for ~75% of U.S. N_2O emissions.[18,19]

Why biotechnology is the right solution at the right time for this opportunity

- Bioengineering of crops has great potential for increasing photosynthetic capture of CO_2 as well as increasing above- and below-ground biomass for carbon storage.

- Engineering of plant-microbe-soil-fertilizer interactions can increase nutrient-use efficiency and enable nitrogen fixation in non-legume crop plants, reducing dependence on synthetic fertilizer.

- Biotechnology can be used to enhance resilience (e.g., water-use efficiency and drought tolerance) in plants, allowing for crop production and GHG capture on marginal or degraded lands.

- Bioengineering can increase protein/nutritional quality in food crops such as soybean, reducing dependence on traditional animal-based food.

- Carbon flux may be altered via metabolic engineering for producing non-food chemicals to promote the bioeconomy.

- Synthetic biology toolboxes are increasingly available and tractable for genome engineering of plants and associated microbes.

- In comparison with traditional breeding, biotechnology has multiple advantages, such as generating more targeted modifications, achieving faster outcomes, and creating new-to-nature traits or functions.

Barriers and gaps that can be addressed with DOE investment/focus

- There are concerns regarding biosecurity of novel, engineered crops as well as public acceptance of plant-based alternatives to traditional animal-based food.

- There are tradeoffs between chemical production and other traits such as whole-plant health and belowground carbon storage.

- There is a lack of deep knowledge for controlling plant metabolism.

- It is challenging to stabilize the root microbiome for *in situ* nitrogen fixation in the field.

- Alternation of plant-microbe-soil interactions must be carefully studied and tested in order to avoid unintended negative consequences.

Cross-cutting approaches needed to address the barriers

- Automation of omics sample preparation and analysis will enable more efficient large-scale data generation for metabolic understanding.

- Development of more automated capabilities will accelerate and streamline data analysis.

- Development of greenhouse and controlled chamber robotics will enable higher-throughput testing and phenotyping in a controlled setting.

- Development of robotics-aided acceleration of genetic improvement of existing crops and identification of new cultivars at lab and field scales.

- Application of AI/ML will improve the development and implementation of biotechnologies for decarbonization, such as identifying biological parts, designing gene circuits, and optimizing plant traits of interest.

Cross-Cutting Advances

In the past decade, new tools and technologies for genome editing have enabled scientists to reimagine the ways in which biotechnology can be performed and applied to solving urgent challenges. CRISPR editing of DNA allows scientists to engineer organisms with precision and fewer off-target effects. The costs for genome sequencing and DNA synthesis are now so low that these technologies are widely available as services for the biotechnology industry. These advances, among others, have dramatically increased scientists' ability to generate large amounts of complex data — and thus the need for increased computation and data science to manage, analyze, and apply this knowledge for genome engineering. A new crop of industrial biotechnology companies has united these new biological tools with artificial intelligence and machine learning (AI/ML) to speed product development time while producing increasing amounts of data that can, in turn, be used to improve machine learning predictions that open new product avenues and further improve the efficiency of biological engineering.

Machine Learning

While the excitement and opportunity for a new phase of biotechnology aided by artificial intelligence and machine learning is growing, the new approaches being pioneered are not widely accessible across the innovation ecosystem and many opportunities remain to be explored. Broader and more accessible application of artificial intelligence and machine learning will enable more accurate predictions of gene function, optimized and novel biological pathways to products, improved process controls for fermentation, ideal microbial communities for agricultural productivity and environmental protection, biomaterials grown to a specification, and many more opportunities yet to be imagined. Previous machine learning successes in automating language translation, detecting tumors, diagnosing skin cancer, and driving cars herald similarly impactful applications to biotechnology.

Workshop participants identified key gaps and barriers in the application of artificial intelligence and machine learning to biotechnology:

- High-quality, standardized data in sufficient quantities to be applied for artificial intelligence and machine learning methods is lacking.

- Experimental design and execution is disconnected from requirements for computation, resulting in data that often cannot be used or reused.

- Integration of disparate and heterogeneous datasets is challenging and in some cases impossible, preventing holistic views of biological systems over time.

- Scale and approaches for artificial intelligence and machine learning are different for biology when compared to other disciplines.

- Many approaches for AI/ML are not built to be "explainable," and thus may not provide useful biological information (e.g., why an approach works) beyond an optimized path to a target.

- Few scientists and researchers are trained in the cross-disciplinary skills at the intersection of biology, chemistry, and AI/ML — nor in the requirements for those approaches.

To overcome these challenges, investment in infrastructure that can support rapid implementation of these techniques is needed, including:

- Dedicated computing hardware appropriate for AI/ML algorithms and methods needed for biotechnology;

- Databases, and databases of databases, that can either store or efficiently connect researchers to heterogeneous data types developed for biology and biotechnology;

- Optimization and development of sensors and sensor networks for data generation in various settings (e.g., fermentation reactors, agricultural fields);

- API standardization for data use and reuse across platforms; and

- Explainable AI/ML methods that provide predictions involving the biological mechanisms that underlie the predictions.

Automation

One of the largest opportunities to fully enable AI/ML for biotechnology broadly across sectors is increased automation for generation of high-quality, standardized data. Companies in the industrial biotechnology sector are increasingly using automation and design-of-experiments to generate the needed information for rapid product development. Despite this, automation is not widely deployed in other research contexts, especially in university and other public-sector research. Challenges related to deployment of automation for automated experiments and experimental design limit the amount of quality data available for AI/ML.

Some of the barriers that can be addressed by the widespread deployment of automation are:

- Most current experimental approaches are rational, that is they rely on human knowledge and hypothesis generation, and do not collect a full range of relevant data (including negative results).

- Only a relatively small number of genes have had a validated function assigned; many annotations are assumptions based on similarity to other genes.

- Biological complexity requires a very large number of experiments to understand biosynthetic pathway design while at the same time, many biological networks and network effects are unknown, leading to challenges in applying new knowledge and predictions to other biosynthetic pathway design.

- Data analysis is often carried out by humans, limiting the speed and transferability of analyses.

- Human operators perform repetitive tasks, an inefficient use of their time and knowledge.

To address these barriers, investment in the development of automated experimentation, data collection, and analysis is needed to rapidly generate the needed data for AI/ML, including investment in the following:

- Miniaturization of experimental approaches, reducing the time, reagents, and cost for experiments while enabling a level of precision only achievable with robots;

- Development of instrumentation that leverages miniaturization for rapid, high-throughput experiments;

- Development and deployment of optimized workflows for automated experiments to ensure comparability of data;

- Increased access to specialized capabilities and facilities, for example biofoundries, for researchers whose needs do not require full-time access to automated experiments; and

- Codevelopment of automated pipelines and machine learning algorithms, so as to fully leverage the predictive power of ML.

Beyond AI/ML and automation, advances across the innovation landscape are needed to accelerate biotechnology solutions:

- Integrated systems analysis (e.g., technoeconomic analysis, life cycle assessments) for AI/ML-driven, biotechnology-based approaches to guide experimentation, development, and deployment;

- Improvement and optimization of bioprocess engineering, including the ability to predict scale-up from small volume fermentations/cultivations to commercial-scale deployment

- Appropriate, hardened cybersecurity practices for biotechnology;

- Development of a trained workforce equally conversant in biotechnology and computing to maximize experimental design, data collection and analysis, and application of AI/ML; and

- Consideration of social and legal issues for biotechnology-based solutions, including energy and environmental justice, economic development, and unintended consequences.

Next Steps

When solutions are accelerated through the integration of machine learning and automation, biotechnology can provide near-, mid-, and long-term reductions in greenhouse gas emissions while supporting the U.S. economy and delivering energy and environmental justice. For these solutions to achieve this impact, coordination and dedicated focus across the innovation ecosystem are required. To develop a strategy for implementation the following activities are recommended:

1. Deep-dive workshops on specific topics to inform implementation on the following topics:

   a. First principles and grand challenges in biology that are broadly enabling for biotechnology

   b. Technical challenges, barriers, and opportunities to integrate artificial intelligence, machine learning, and automation across industrial biotechnology, from basic science to deployed technologies

   c. Integration of systems analysis, especially for unproven or unknown approaches, in AI/ML-guided biotechnology solutions

   d. Workforce development and incentives for integrating multidisciplinary teams, and technology transitions of biotechnology solutions to commercialization

2. A 5-year research and development strategy developed from workshop findings

   a. Near-, mid-, and long-term opportunities for impact on GHG emissions

   b. Enabling technologies to accelerate time to impact for those opportunities

   c. Sustaining infrastructure for the public good (e.g., biofoundries, databases, training programs)

APPENDIX B:
DESIGNING THE BIOECONOMY FOR DEEP DECARBONIZATION WORKSHOP AGENDA AND PARTICIPANTS

Designing the Bioeconomy for Deep Decarbonization

Applying Biotechnology to Solve Challenging Problems in Transportation, Industry, and Agriculture

Opportunities and Impacts Workshop | April 30, 2021

11:30 am–3:30 pm EDT | 8:30 am–12:30 pm PDT

Virtual: Zoom + Miro

Workshop Agenda

Time	Topic	Speaker
12:10 pm EDT/ 9:10 am PDT	**Plenary presentation:** Opportunities and impacts for the agricultural sector *15 minutes*	**Corinne Scown** Staff Scientist & Deputy Director for Research, Energy Analysis & Environmental Impacts Division, Lawrence Berkeley National Laboratory
11:40 am EDT/ 8:40 am PDT	**Plenary presentation:** Opportunities and impacts for the transportation sector *15 minutes*	**Lee Lynd** Paul E. and Joan H. Queneau Distinguished Professor of Engineering, Dartmouth College
11:55 am EDT/ 8:55 am PDT	**Plenary presentation**: Opportunities and impacts for the industrial sector *15 minutes*	**Brent Shanks** Anson Marston Distinguished Professor in Engineering, Mike and Jean Steffenson Chair, Iowa State University
12:10 pm EDT/ 9:10 am PDT	**Plenary presentation:** Opportunities and impacts for the agricultural sector *15 minutes*	**Corinne Scown** Staff Scientist & Deputy Director for Research, Energy Analysis & Environmental Impacts Division, Lawrence Berkeley National Laboratory

Time	Topic	Speaker
12:25 pm EDT/ 9:25 am PDT	**Facilitation tool practice activity** *10 minutes*	**Katy Christiansen** Head, Biosciences Strategic Programs Development Group, Lawrence Berkeley National Laboratory
12:35 pm EDT/ 9:35 am PDT	**BREAK** *10 minutes*	
12:45 pm EDT/ 9:45 am PDT	**Breakout session #1:** Answer charge questions for each priority topic (see breakout questions below) (concurrent discussions in breakout groups) *60 minutes*	**Participants will be assigned to one of three topical groups:** • Transportation • Industry • Agriculture
1:45 pm EDT/ 10:45 am PDT	**Report out for breakout session #1** *15 minutes*	**Session chairs**
2:00 pm EDT/ 11:00 am PDT	**BREAK** *10 minutes*	
2:10 pm EDT/ 11:10 am EDT	**Breakout session #2:** Answer charge questions for each priority topic (see breakout questions below) (concurrent discussions in breakout groups) *40 minutes*	**Participants will remain with their topical groups:** • Transportation • Industry • Agriculture
2:50 pm EDT/ 11:50 am PDT	**Report out for breakout session #2** *15 minutes*	**Session chairs**
3:05 pm EDT/ 12:05 am PDT	**Next steps and wrap up** *15 minutes*	
3:20 pm EDT/ 12:20 pm PDT	**Workshop concludes**	

Breakout Session Facilitators

Transportation

Aindrila Mukhopadhyay, Biological Engineer Senior Scientist, Lawrence Berkeley National Laboratory

Héctor García Martín, Staff Scientist, Lawrence Berkeley National Laboratory

(Miro support: **Katy Christiansen**)

Industry

Scott Nicholson, Researcher II-Chemical Engineering, National Renewable Energy Laboratory

Jon Magnuson, Senior Research Scientist, Pacific Northwest National Laboratory

(Miro support: **Phil Lee**)

Agriculture

Scott Baker, Functional and Systems Biology Science Area Lead, Environmental Molecular Sciences Laboratory, Pacific Northwest National Laboratory

Xiaohan Yang, Senior Scientist, Oak Ridge National Laboratory

(Miro support: **Lauren Jabusch**)

Charge Questions

In your breakout groups, you will be asked to identify specific applications of biotechnology that have the potential for the largest impact on reducing GHG emissions for transportation, industry, and agriculture. For the breakout sessions, you will be asked the following questions.

Breakout #1: Identification of the challenge/opportunity

- Why is biotechnology uniquely suited to address the challenge?

- What is the likely scale of impact of the opportunity in terms of GHG reductions?

- What are the barriers and gaps in the application of biotechnology to realize the opportunity?

- What is the timescale for development to make a significant impact?

Breakout #2: Identification of cross-cutting advances in areas (such as machine learning and automation) that are needed to increase the speed and efficiency with which biotechnology can have an impact in decarbonization

- What gap is being addressed and how will that accelerate the impact of biotechnology?

- What infrastructure needs exist?

- What is the timescale for development/implementation?

- Why is now the right time for this opportunity and what are the risks of not pursuing it?

Participants (by first name)

First name	Last name	Breakout group assignment
Ada	Sedova	Agriculture
Anthe	George	Transportation
Brent	Shanks	Industry
Corinne	Scown	Agriculture
Daniel	Northrup	Agriculture
Deepti	Tanjore	Industry

First name	Last name	Breakout group assignment
Eric	McAfee	Transportation
Gale	Wichmann	Industry
Huimin	Zhao	Transportation
India	Hook-Barnard	Transportation
Jim	Bielenberg	Transportation
Karen	Draths	Industry
Kim	Hixson	Agriculture
Lee	Lynd	Transportation
Leslie	Snowden-Swan	Transportation
Lieve	Laurens	Transportation
Michael	Koepke	Transportation
Nathan	Hillson	Industry
Nolan	Wilson	Industry
Paul	Bryan	Transportation
Philip	Laible	Industry
Raychel	Santo	Agriculture
Saga	Mundree	Agriculture
Sarah	Teter	Industry
Scott	Nicholson	Industry
Shilpa	Raja	Agriculture
Stan	Martin	Agriculture
Stephen	Long	Agriculture
Steve	Strauss	Agriculture
Sunil	Chandran	Transportation
Thathiana	Benavides	Transportation

Participating DOE Staff

Bioenergy Technologies Office

Gayle Bentley

Jay Fitzgerald

Phil Lee (Allegheny Science & Technology)

Valerie Reed

Joel Sarapas (AAAS Science and Technology Policy Fellow)

Office of Biological and Environmental Research

Todd Anderson

Wayne Kontur (AAAS Science and Technology Policy Fellow)

Advanced Research Projects Agency — Energy

David Babson

Office of Advanced Scientific Computing Research

Steven Lee

Office of Science

Michael Cooke

U.S. DEPARTMENT OF ENERGY

APPENDIX C: REFERENCES

1. U.S. Energy Information Administration. Annual Energy Outlook 2020. https://www.eia.gov/outlooks/aeo/.

2. Nicholson, S. R., Rorrer, N. A., Carpenter, A. C. & Beckham, G. T. Supply chain energy and greenhouse gas emissions associated with petrochemical manufacturing in the United States.

3. Carr, M., Brown, T. & Murphy, C. Examining biotechnology's contributions to addressing the climate crisis. *BIO Biotechnology Industry Organization* (2021).

4. Committee on Accelerating Decarbonization in the United States, Board on Energy and Environmental Systems, Division on Engineering and Physical Sciences & National Academies of Sciences, Engineering, and Medicine. *Accelerating decarbonization of the U.S. energy system.* (National Academies Press, 2021). doi:10.17226/25932.

5. Office of Transportation and Air Quality. *U.S.Transportation Sector Greenhouse Gas Emissions.* (2020).

6. Baral, N. R. *et al.* Techno-economic analysis and life-cycle greenhouse gas mitigation cost of five routes to bio-jet fuel blendstocks. *Energy Environ. Sci.* **12,** 807–824 (2019).

7. Rogers, J. N. *et al.* An assessment of the potential products and economic and environmental impacts resulting from a billion ton bioeconomy. *Biofuels, Bioprod. Bioref.* **11,** 110–128 (2017).

8. U.S. Environmental Protection Agency. Greenhouse Gas Reporting Program (GHGRP) Chemicals. https://www.epa.gov/ghgreporting/ghgrp-chemicals (2020).

9. Nicholson, S. R., Rorrer, N. A., Carpenter, A. C. & Beckham, G. T. Manufacturing energy and greenhouse gas emissions associated with plastics consumption. *Joule* (2021) doi:10.1016/j.joule.2020.12.027.

10. FAO. World fertilizer trends and outlook to 2022. http://www.fao.org/publications/card/en/c/CA6746EN/ (2019).

11. U.S. Environmental Protection Agency. Inventory of U.S. Greenhouse Gas Emissions and Sinks: 1990-2019. https://www.epa.gov/ghgemissions/inventory-us-greenhouse-gas-emissions-and-sinks-1990-2019.

12. Ahmed, J. *et al.* Agriculture and climate change: Reducing emissions through improved farming practices. *McKinsey & Company* (2020).

13. Smith, P. *et al.* Agriculture, forestry and other land use (AFOLU). in *Climate Change 2014: Mitigation of Climate Change. Contribution of Working Group III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change* (eds. Edenhofer, O. *et al.*) (Cambridge University Press, 2014).

14. Sutton, M. A. et al. Nitrogen - Grasping the Challenge. A Manifesto for Science-in-Action through the International Nitrogen Management System.Summary Report. *Centre for Ecology & Hydrology, Edinburgh, UK* (2019).

15. Gerber, P. J. & Food and Agriculture Organization of the United Nations. Tackling Climate Change Through Livestock: *A Global Assessment Of Emissions And Mitigation Opportunities.* 141 (Food & Agriculture Organization, 2014).

16. Huang, H., Long, S. & Singh, V. Techno-economic analysis of biodiesel and ethanol co-production from lipid-producing sugarcane. *Biofuels, Bioprod. Bioref.* **10,** 299–315 (2016).

17. Unable to find information for 11176971.

18. Brown, T. Ammonia production causes 1% of total global GHG emissions. https://ammoniaindustry.com/ammonia-production-causes-1-percent-of-total-global-ghg-emissions/ (2016).